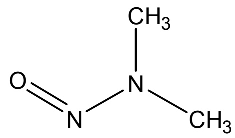
# *N*-NITROSODIMETHYLAMINE
**CAS No. 62-75-9**

First Listed in the *Second Annual Report on Carcinogens*



## CARCINOGENICITY

*N*-Nitrosodimethylamine is *reasonably anticipated to be a human carcinogen* based on sufficient evidence of carcinogenicity of in experimental animals (IARC V.17, 1978; IARC S.4, 1982). When administered orally, *N*-nitrosodimethylamine induced liver hemangiosarcomas, hepatocellular carcinomas, and kidney and lung tumors in mice. When mice were exposed by inhalation, the compound induced tumors in the lung, liver, and kidney. When administered by intramuscular injection, the compound induced hemangiosarcomas of the liver and abdominal tissues and lung tumors in adult mice and parenchymal cell and vascular tumors of the liver and lung adenomas in new born and suckling mice. When administered by intraperitoneal injection, the compound induced liver tumors in adult and newborn mice and increased the incidence of lung and kidney tumors in mice. When administered orally, *N*-nitrosodimethylamine induced kidney and bile duct tumors in rats and when rats were exposed by inhalation, it induced tumors of the lung, liver, kidney and nasal cavity. When administered by intramuscular injection, the compound induced kidney tumors in adult rats and kidney and liver tumors in newborn and suckling rats, and it induced kidney and nasal cavity tumors in rats when administered by intraperitoneal injection. When administered orally, *N*-nitrosodimethylamine induced hepatocellular carcinomas and bile duct tumors in hamsters, and when administered by intramuscular injection, it induced hemangiosarcomas in the liver and bile duct and nasal cavity tumors in hamsters. When administered orally, the compound induced hepatocellular carcinomas and bile duct tumors in rabbits and guinea pigs, liver hemangiosarcomas in ducks, and liver adenomas and adenocarcinomas in fish. When administered by intramuscular injection, the compound induced bile duct tumors in mastomys and when administered by intraperitoneal injection, it induced liver tumors in newts.

There are no adequate data available to evaluate the carcinogenicity of *N*-nitrosodimethylamine in humans (IARC V.17, 1978; IARC S.7, 1987).

## PROPERTIES

*N*-Nitrosodimethylamine is a volatile, yellow, oily liquid of low viscosity. It is soluble in water, alcohol, ether, other organic solvents, and lipids. The compound is sensitive to light, especially ultraviolet light and undergoes relatively rapid photolytic degradation. *N*-Nitrosodimethylamine is combustible and when heated to decomposition, it emits toxic fumes of nitrogen oxides ($NO_x$). It is incompatible with strong oxidizers and strong bases.

## USE

*N*-Nitrosodimethylamine is used primarily as a research chemical. Prior to April 1, 1976, the compound was used as an intermediate in the electrolytic production of 1,1-dimethylhydrazine, a storable liquid rocket fuel that contained approximately 0.1% *N*-nitrosodimethylamine as an impurity. Other uses of *N*-nitrosodimethylamine include the control of nematodes, inhibition of nitrification in soil, plasticizer for rubber and acrylonitrile polymers, in active metal anode-electrolyte systems (high-energy batteries), in the preparation of thiocarbonyl fluoride polymers, as a solvent in the fiber and plastics industry, an antioxidant, a softener of copolymers, and as an additive to lubricants (Sittig, 1985; Merck, 1983).

## PRODUCTION

Current production data are not available and there is no evidence that *N*-nitrosodimethylamine is manufactured commercially in the United States (IARC V.17, 1978). The 1979 TSCA Inventory reported four U.S. companies producing 1,000 lb in 1977 with some site limitations. The CBI Aggregate was < 1 million lb. No import or export data were reported (TSCA, 1979). The last commercial producer of *N*-nitrosodimethylamine closed its plant in 1976. Commercial production began in the mid-1950s for use in the manufacture of 1,1-dimethylhydrazine (IARC V.17, 1978).

## EXPOSURE

The primary routes of potential human exposure to *N*-nitrosodimethylamine are ingestion, inhalation, and dermal contact. There is some potential for occupational exposure of laboratory, copolymer, lubricant, and pesticide workers in the workplace. The National Occupational Exposure Survey (1981-1983) indicated that 747 workers, including 299 women, were potentially exposed to *N*-nitrosodimethylamine (NIOSH, 1984). ACGIH regards *N*-nitrosodimethylamine as a suspected carcinogen and recommends no exposure or minimal exposure to the compound (ACGIH, 1986). OSHA regulations concerning *N*-nitrosodimethylamine designate strict procedures to avoid worker contact. Mixtures containing ≥ 1.0% *N*-nitrosodimethylamine must be maintained in isolated or closed systems, workers must observe special hygiene rules, and certain procedures must be followed for movement of the material and in case of accidental spills and emergencies. Synthetic cutting fluids, semisynthetic cutting oils, and soluble cutting oils may contain nitrosamines, either as contaminants in amines or as products from reactions between amines and nitrite. Concentrations of nitrosamines have been found in certain synthetic cutting oils at levels ranging from 1 to 1000 ppm. There are approximately 8-12 additives that could be responsible for nitrosamine formation in cutting oils. Approximately 750,000 to 780,000 workers employed by more than 1,000 cutting fluid manufacturing firms are potentially exposed to nitrosamines in cutting oils. In addition, there is potential exposure of an undetermined number of machine shop workers who use these fluids. The general population may possibly be exposed to unknown quantities of *N*-nitrosodimethylamine present in foods and beverages, tobacco smoke, herbicides, pesticides, drinking water, and industrial pollution. Estimates indicate that air, diet, and smoking contribute to potential human exposure at levels of a few micrograms per day. *N*-Nitrosodimethylamine is present in a variety of foods including cheeses, soybean oil, canned fruit, various meat products, bacon, various cured meats, frankfurters, ham (cooked), fish and fish products, spices used for meat curing, apple brandy, other alcoholic beverages, and beer. Concentrations in these foodstuffs have been measured to be between 0 and 85 µg/kg. FDA and CPSC have determined that *N*-nitrosamines, such as *N*-nitrosodimethylamine, are frequently produced during rubber processing and may be present as contaminants in the final rubber product. Potential exposure depends on the ability of the nitrosamine to migrate from the product into the body. *N*-Nitrosodimethylamine has been detected in numerous drugs formulated with aminopyrine including tablets, suppositories, injections, drops, and syrups at concentrations ranging from < 10 to 371 µg/kg. *N*-Nitrosodimethylamine has been detected in tobacco smoke at concentrations of 0-140 ng/cigarette. Mainstream smoke of nonfiltered cigarettes contained 13-65 ng/cigarette, and 5.7-43 ng/cigarette for filtered cigarettes. Sidestream smoke of nonfiltered cigarettes contained 680-823 ng/cigarette, and 1040-1770 ng/cigarette for filtered cigarettes. An analysis of smoke-filled rooms, such as bars, indicated concentrations of 90-240 ng/$m^3$ *N*-nitrosodimethylamine, and residences contained < 5 ng/$m^3$. Indoor air polluted with tobacco smoke has been shown to contain up to 0.24 ng/l *N*-nitrosodimethylamine (HEEP, 1980).

*N*-Nitrosodimethylamine is widespread in the environment, but it is rapidly decomposed by sunlight and thus does not usually persist in ambient air or water illuminated by sunlight (HEEP, 1980). *N*-Nitrosodimethylamine was detected as an air pollutant in Baltimore, Maryland, and in Belle, West Virginia. In Baltimore, the prime source was found to be a chemical plant that manufactured 1,1-dimethylhydrazine. The concentration of *N*-nitrosodimethylamine at the factory ranged from 6,000 to 36,000 ng/$m^3$, 1000 ng/$m^3$ in adjacent residential neighborhoods, and about 100 ng/$m^3$ two miles away in downtown Baltimore. This plant was closed in April 1976. In Belle, the source of the *N*-nitrosodimethylamine was found to be a chemical factory manufacturing and using dimethylamine; the *N*-nitrosodimethylamine was being produced as an unwanted by-product. Concentrations in downtown Belle and Charleston ranged from 1 to 40 ng/$m^3$. Similar concentrations of *N*-nitrosodimethylamine have been detected at chemical factories making and/or using dimethylamine, including plants in New York City, Boston, and New Jersey. *N*-Nitrosodimethylamine has been detected in sea water adjacent to the Baltimore factory at concentrations of 0.08-0.25 µg/l and in an adjacent sewage treatment facility at 3.0 µg/l. Industrial wastewater from chemical factories was found to contain 0.2-5 µg/l (IARC V.17, 1978). *N*-Nitrosodimethylamine has been detected in deionized water at concentrations of 0.012-0.34 µg/l, in high-nitrate well water at < 0.01 µg/l, and in chlorinated drinking water at 0.02-0.82 µg/l. Soil samples taken from locations near industrial plants contained 0-15.1 ng/g *N*-nitrosodimethylamine. Dimethylamine-formulated pesticides and herbicides were found to contain 190-640 mg/l (IARC V.17, 1978). Significant levels of *N*-nitroso compounds have been identified in a number of materials including pesticides, cosmetics, drugs, cutting fluids, and fire-resistant hydraulic fluids. The *N*-nitroso compounds found in these products were apparently formed in situ during storage or handling as the result of a reaction between amines present in the mixture and inorganic nitrite, which may have been added as a corrosion inhibitor (CHIP, 1978). Additional exposure information may be found in the ATSDR Toxicological Profile for *N*-Nitrosodimethylamine (ATSDR, 1989d).

## REGULATIONS

EPA regulates *N*-nitrosodimethylamine under the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA), which established a reportable quantity (RQ) of 10 lb. EPA also regulates *N*-nitrosodimethylamine under the Resource Conservation and Recovery Act (RCRA) as a constituent of hazardous waste, and under the Clean Water Act (CWA) with respect to accidental releases of the compound. The water quality criteria document for nitrosamines, published under CWA, includes *N*-nitrosodimethylamine. The Superfund Amendments and Reauthorization Act (SARA) identifies *N*-nitrosodimethylamine as an extremely hazardous substance and establishes threshold planning quantities and facility notification responsibilities for state and local emergency response plans. SARA also subjects *N*-nitrosodimethylamine to reporting requirements and requires the preparation of its toxicological profile. Under the Toxic Substances Control Act (TSCA), EPA has prohibited the addition of nitrites to fluids used in metal cutting if they contain triethanolamine salt, tricarboxylic acid, or a tricarboxylic acid intermediate. An enforcement policy was issued by CPSC announcing that the Commission may take action against pacifiers entering interstate commerce that contain more than 60 ppb nitrosamines. These studies have determined the presence of specific nitrosamines, including *N*-nitrosodimethylamine, in pacifiers and nipples, and the amounts released into saliva stimulant and food. FDA has set a 10-ppb limit on nitrosamines in rubber nipples for baby bottles. An ASTM standard has been developed which sets the level of nitrosamines in pacifiers at 10 ppb for any individual nitrosamine. FDA also established action levels of 5 ppb *N*-nitrosodimethylamine in malt beverages and 10 ppb in barley malt, which is expected to reduce or eliminate exposure from these sources. OSHA promulgated a standard for *N*-nitrosodimethylamine that includes requirements for protective clothing, respirators, medical surveillance, and engineering controls. OSHA regulates *N*-nitrosodimethylamine under the Hazard Communication Standard and as a chemical hazard in laboratories. Regulations are summarized in Volume II, Table B-102.